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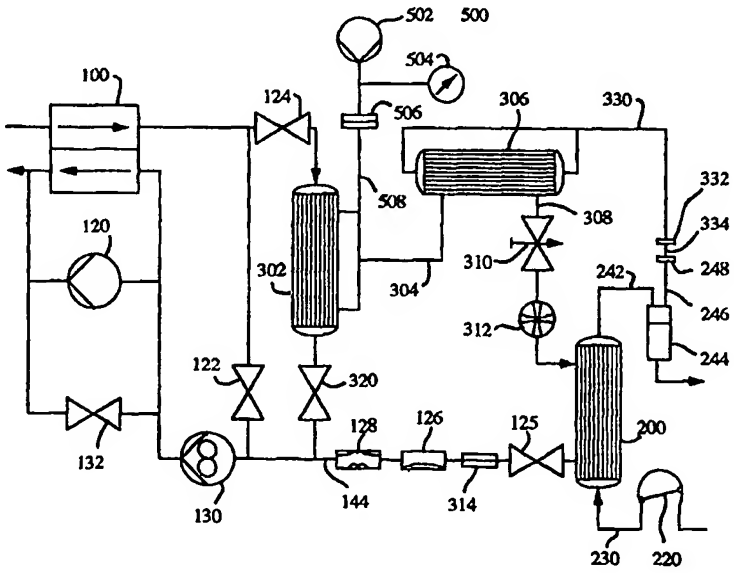

(57) Abstract

There is described a device for hemodiafiltration with a fluid balancing device and on–line preparation of the substitution fluid from dialysate by sterile filters. The preferred embodiment uses two sterile filters whereby the first filters the dialysate and the second is passed by the dialysate. This second sterile filter is arranged in the dialysate fluid circuit between the first filter and the dialyser in a positive pressure area, which is separated from the rest of the downstream dialysate circuit. Due to the positive pressure in the area of the second filter, the dialysate passes through the filter membrane and from there to the extracorporeal circuit via a line as substitution solution.

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Device and method for preparation of substitution solution

AREA OF INVENTION

The present invention relates to a method and device for producing a substitution fluid for use during hemodiafiltration or hemofiltration in a hemodialysis machine or for use as filling and rinsing fluid during preparation of a hemodialysis machine.

PRIOR ART

A hemodialysis treatment is used for treating patients having acute or chronic renal insufficiency. Blood is taken out from the patient in an extracorporeal blood circuit and passes through a dialyser that removes uraemic toxins in the blood and reconstitutes the blood by balancing electrolytes, such as sodium, potassium, calcium, magnesium etc., and adding necessary substances, such as bicarbonate. Moreover, a certain amount of fluid is removed from the blood , called ultrafiltrate, since the patient cannot get rid of superfluous fluid the normal way. Hemodialysis uses mainly diffusion through a semipermeable membrane for performing the treatment.

Another treatment modality that has been more used lately is hemofiltration, whereby the blood is filtered in a hemofilter and the filtrate is discarded. Substitution fluid is added, before or after the filtration for replacing the discarded ultrafiltration fluid. Hemofiltration uses mainly convection for removing the ureamic toxins and the substitution fluid comprises the necessary electrolytes for balancing and addition purpose. A smaller amount of substitution fluid is added compared to the removed ultrafiltrate fluid for removing the necessary fluid from the patient.

Another treatment modality, which is a combination of hemodialysis and hemofiltration is called hemodiafiltration and is essentially a combination of these two treatment modalities and uses a hemodiafilter.

These treatment methods are described in numerous text books and it is not necessary to describe them in more details in the present specification. One description is in the chapter: "Hemodialysis Machines and Monitors" by Polaschegg HD, Levin NW in " Replacement of renal function by dialysis", by Jacobs C, Kjellstrand CM, Koch KM, Winchester JF, 4th ed. Kluwer academic publishers, 1996:333-79.

The above-mentioned substitution fluid can be prepared as a pharmaceutical solution, which however is expensive. Therefore, it is preferred to produce the substitution solution on-line on the dialysis machine by filtration of the dialysis fluid. However, the preparation method needs to be adapted for preparing a substitution fluid that is sterile and can be used for infusion purpose.

Thus, a dialysis machines adapted for hemofiltration and hemodiafiltration also includes a device for preparing the substitution fluid on-line. This device usually comprises two filters for producing the substitution fluid for securing the sterility of the prepared fluid.

Some patent specifications describing devices of interest for the present invention are: DE 2944136 (US 4209391, Cordis Dow), EP 189561(DE 3444671, Fresenius), DE 3448262 (Fresenius), EP 270794 (DE 3641843, US 4834888, Fresenius), EP 407737 (DE 3923078, Fresenius), DE 4240681 (Fresenius), EP692268 (Fresenius), EP 165519 (Gambro), EP 694312 (Hospal) and EP 745213 (Gambro).

DISCLOSURE OF THE INVENTION

Previous dialysis machines for producing on-line substitution solutions comprises a peristaltic pump arranged at the front of the dialysis machine for propelling the substitution fluid. A peristaltic pump comprises several rollers interacting with a plastic tube pump segment and occluding the pump segment. By moving the roller along the tube while occluding the tube, the fluid is pumped. The substitution fluid flow rate is approximately proportional to the rotational speed of the peristaltic pump.

The peristaltic pump is used since it can easily be placed on the front of the machine and co-operates with a tube portion that can be produced as a sterile article. However, the tube portion used has a limited life time. Thus, the pump segment and the second filter needs to be replaced, for example after one month, which means comparatively high costs. Also the peristaltic pump involves costs and uses a relatively large additional space on the front of the machine. This peristaltic pump is placed on the front since the pump segment must be replaced regularly. All these makes the preparation for the treatment complicated.

If the peristaltic pump is used with a disposable tube system and disposable second filter, the disposable tube system needs to comprise a pump segment and the second filter. Thus, such a disposable tube system is comparatively expensive and bulky.

The object of the present invention is to provide a method and a device which obviates the drawbacks of the prior art dialysis machines.

Another object of the invention is to provide a dialysis machine for producing substitution fluid on-line, in which the peristaltic pump previously used is dispensed of.

According to the invention, such a method and device involves the fact that the second filter is arranged in a portion of the dialysis fluid circuit which always is under positive pressure. By this positive pressure, a filtration of the substitution solution takes place without the use of an additional pump.

A machine which includes a device for obtaining an positive pressure is disclosed in for example the patent specification with inventors Lipps Ben J., Landau Julian I., and applicant Cordis Dow Corp. Moreover, such a previously known dialysis machine is AK-100 Ultra sold by GAMBRO AB.

SHORT DESCRIPTION OF THE DRAWINGS

Further objects, advantages and features of the invention appears from the following description of several embodiments of the invention with reference to the appended drawings.

Fig. 1 is a schematic diagram of a first embodiment of the invention.

Fig. 2 is a schematic diagram of a second embodiment of the invention.

Fig. 3 is a schematic diagram of the first embodiment of the invention, but adapted for testing the integrity of the filter membranes.

Fig. 4 is a schematic diagram of a third embodiment of the invention.

Fig. 5 is a schematic diagram of a fourth embodiment of the invention.

DETAILED DESCRIPTION OF THE EMBODIMENTS

Figure 1 discloses a first embodiment of the invention, comprising a balancing system 100 for a dialysis fluid.

By the expression balancing system is intended a system that works with balancing chambers or balancing pistons, such as for example in the machines series 2008 or 4008 by the company Fresenius, the machine Centry 3 of company Cobe, the machine System 1000 of company Althin Medical, the machine MIROCLAV of company Baxter Deutschland or the machine DIALOG of company B. Braun-Melsungen. The expression also comprises a

balancing system that works with flow meters, such as for example the machine Integra of company Hospal. These balancing systems make sure that the inlet and outlet amounts are equal, and that is why they often are called "flow equaliser" in the US patent literature. In these balancing systems, fluid is removed from the patient by a parallel connected ultrafiltration pump 120.

However, the invention can also be used with a balancing system that produces a predetermined inlet and outlet flow rate differential without additional ultrafiltration pumps, such as for example the machine AK100 of company Gambro, see for example EP 278100. The inlet flow to the dialyser is slightly smaller than the outlet flow from the dialyser and the difference makes the ultrafiltration.

The fresh dialysis fluid from the balancing system 100 passes through a concentration and temperature monitor (not shown) and also through a dialysis valve 124 to a first sterile filter 302 comprising a semipermeable membrane. The dialysis valve together with the concentration and temperature monitor and the bypass valve 122 act as a security system and prevents dialysis with wrong dialysis fluid composition and/or temperature. These devices belongs to the state of the art.

For rinsing or flushing the sterile filter, the dialysis fluid can flow along the membrane of the filter and via a valve 320 and to the outlet.

When the valve 320 is closed, the dialysis fluid passes through the membrane of the sterile filter 302 to a line 304 for producing a clean dialysis fluid. From line 304, the dialysis fluid reaches a second sterile filter 306 and passes along the membrane to an outlet line 308, without being filtered. Line 308 is normally connected to a dialyser 200, which also can be a hemofilter or a hemodiafilter as mentioned above.

Line 308 comprises a throttle device or throttle valve 310 between the second filter and the dialyser. Moreover, line 308 comprises a flow sensor 312.

The dialysis fluid also passes through the membrane of the second sterile filter 306 to produce a sterile substitution fluid in line 330 to be supplied to the blood in an extracorporeal circuit to be described below. Thus, the flow from the first filter 302 is measured or controlled by the balancing unit 100 and then divided in a first flow to the dialyser via throttle valve 310 and flow sensor 312 and a second substitution fluid flow via line 330 and to the blood of the patient. It is desired to control the flow of substitution flow to obtain the goals of the treatment. By measuring the total flow and the flow to the dialyser, the substitution flow must

always be the difference between these flows. A control unit (not shown) adjusts the throttle device so that the desired substitution fluid flow is obtained.

The throttle valve 310 can be a constant pressure valve, which guaranties a constant upstream pressure independent of the flow passing there through. The substitution flow is thereby given by the pressure difference relative to the extracorporeal circuit and the filtration resistance of the sterile filter 306.

Alternatively, the throttle valve 310 can be a constant flow valve, which is adjusted to a certain fluid flow rate which is equal to the flow through the balancing system minus the intended substitution flow. By means of such a valve, there is automatically obtained a pressure which results in the desired substitution fluid flow.

The throttle valve can in a further alternative be an adjustable throttle valve which is controlled by a control device not shown. The flow meter 312 is arranged downstream of the throttle device 310 but can alternatively be arranged upstream of the throttle device but downstream or the second sterile filter 306. This flow meter reads the difference between the dialysate flowing through the balancing unit 100 and the substitution fluid. Since the flow passing through the balancing unit is either predetermined or measured, the substitution fluid flow can be indirectly measured by the flow meter 312. By means of this information, the throttle device 310 can be adjusted, manually or by means of a control unit (not shown), so that the desired substitution fluid flow is obtained.

Moreover, the throttle device can be a three-way valve adjusted so that the desired proportion of flows are obtained.

The spent dialysis fluid, called the dialysate, leaves the dialyser 200 through a line 144, comprising a second dialyser valve 125 as well as a bypass connector (male or female) 314. Moreover, line 144 comprises a dialysate pressure sensor 126 and a blood leak detector 128. The spent dialysate passes through the balancing system by means of a dialysate circulation pump 130 and further to the drain.

Parallel to the balancing system 100 there is another valve 132, which makes possible the separation of air, since many balancing systems are disturbed by air. This valve is controlled by an air detection system (not shown).

The dialysis fluid in the second filter 306 has a positive pressure relative to the atmosphere and to the extracorporeal circuit and is filtered through the membrane of the filter. Via line 330 the filtered and sterile substitution fluid reaches a drip chamber connector 248.

Line 330 terminates in a male connector 332 attached to an anticontamination intermediate portion 334, which via a line 246 is connected to a venous drip chamber 244 of the extracorporeal circuit.

The extracorporeal circuit comprises according to known technique a blood pump 220, an arterial tube system 230, the blood portion of the dialyser 200 and a venous tube system 242 incorporating the venous drip chamber 244. The embodiment shown in Fig.1 is a "post-dilution" device, i.e. the substitution fluid is introduced after the dialyser and the blood is diluted after the dialyser. Alternatively, the substitution fluid can be introduced before the dialyser (pre-dilution), between two dialysers (mid-dilution), before and after, respectively before-between-after the dialysers. The substitution solution can also be introduced before the blood pump in the negative pressure area. The advantage of such a method is that a larger pressure gradient is available for the filtration in sterile filter 306 and that the arterial tube system is driven with a higher flow and diluted blood, which decreases the viscosity, see DE 4240681 filed August 8, 1994.

Fig. 5 discloses a slightly modified embodiment of the present invention. Instead of the balancing system 100, there is used two adjustable constant flow pumps 401 and 403 and two flow meters 402 and 404. The first constant flow pump 401 passes about 500 ml/min of dialysis fluid. The second constant flow pump 403 passes about 520 ml/min and the difference there between accounts for the ultrafiltration and is controlled by the computer of the dialysis machine. The flow meters 402 and 404 are used for measuring the ultrafiltration by calculating the differential flow rate, i.e. 20 ml/min with the above-mentioned figures. It is clear that the above-mentioned figures of flow rates are only exemplary and that other values can be used. Generally, the dialysis flow rate is 300 - 700 ml/min and the ultrafiltration is about 1000 - 4000 ml per treatment. Each treatment usually last during 3 - 5 hours, three times per week.

From the first constant flow meter 401, the dialysis fluid passes a clean dialysate filter 405 and enters a line 406 leading to the dialyser 200. Line 406 further comprises a branch line 408 leading to a sterile filter 409, the outlet of which is connected to the substitution line 330 according to the previous embodiments. From the dialyser 200, the dialysate passes through different devices disclosed as a box 412, such as a blood leak detector, and further to said flow meter 404 and constant flow pump 403 and finally to the drain.

Line 408, sterile filter 409 and line 330 are made as a disposable unit integral with the remaining extracorporeal circuit, such as drip chamber 244, line 242, line 230 and pump

segment 220. By the present invention, said disposable unit can be made without one pump segment, which decreases the costs and complexity significantly. The disposable unit is sterilised during the manufacturing process. Since sterile filter 409 is used only once, it can be made much smaller as indicated in Fig. 5.

Line 406 comprises a third constant flow pump 407 which is adjusted to for example 350 ml/min, which is the difference between the dialysis flow (500 ml/min) and the desired substitution flow (150 ml/min). The constant flow pumps operate for providing the pressures necessary for obtaining the adjusted flow rates. Thus, the pressure inside the dialyser is adjusted to a negative pressure compared to the blood pressure inside the dialyser to provide a desired ultrafiltration. Moreover, the pressure at the branch line 408 is a positive pressure necessary for passing the desired amount of substitution fluid through the membrane of filter 409. A pressure sensor 413 is arranged at the branch connection to monitor the pressure before the sterile filter 409. If the pressure is outside a predetermined pressure value, an alarm signal is generated, indicating for example blocked sterile filter, as described in Swedish Patent application No. 9703403-7 filed September 22, 1997, applicant Gambro AB.

For rinsing filter 405, there is provided a valve 410 between a second outlet of the filter and line 406. If the valve 410 is opened and the dialyser is bypassed by a bypass valve 411, the dialysis fluid passes through the filter in parallel with the membrane to rinse away possible contaminations on the surface of the membrane.

Fig. 5 discloses a dialysis machine adapted for hemodiafiltration when purification of the blood takes place both by dialysis (diffusion) and by filtration (convection). It is possible to adapt the machine to hemofiltration by opening valve 411 and closing a valve positioned in the line from the constant flow pump 407 to the upper connection to the dialyser in Fig. 5. The dialyser 200 is replaced by a hemofilter having only the lower connection to the dialysis fluid circuit seen according to Fig. 5. The constant flow pumps 401, 403 and 417 will adjust the different flows to obtain the desired conditions for the hemofiltration. One possibility is to have the following flows: pump 401: 500 ml/min; pump 403: 515 ml/min; and pump 417: 300 ml/min, resulting in a substitution flow of 200 ml/min. Another possibility is to have the following flows: pump 401: 200 ml/min; pump 403: 215 ml/min; and pump 417: 0 ml/min, resulting in a substitution flow of 200 ml/min. In the last case, the pump 417 can be replaced by a valve or throttle, being closed. A skilled person realises further modifications.

The sterile filters 302 and 306 and also dialyser 200 can be controlled for the integrity

of the membrane by means of a pressure retention test in a test system 500. Such a test method is described in for example DE 3923078.

A test of the sterile filter will be described with reference to Fig.2.

Fig. 2 discloses a second embodiment modified in relation to figure 1, such as described in DE 3641843 (US 4834888). The dialyser valve is placed between the first 302 and the second 306 sterile filters. The dialysis fluid line 308 and dialysate fluid line 144 are interconnected by a short-circuit portion 150. The substitution fluid line 330 with the anticontamination portion 334 is connected to the dialysate line 144 downstream of the second dialyser valve 125 via the bypass connector 314.

For testing the integrity of the membranes of the sterile filers, the bypass valve 122, the first dialyser valve 124 and the bleeding valve 132 are opened and the second dialyser valve 125 is closed. Pump 502 urges air into the line 304 between the first 302 and the second 306 sterile filters. Thereby, the dialysis fluid is pressed away, at one side via valve 122 and at the other side via line 330 and reaches the dialysate line 144 and then via pump 130 and valve 132 to the drain. At intact sterile filter membranes, this operation terminates when all fluid has been removed from line 304 between the sterile filters and the interior of the filters up to the membranes, since air can pass the hydrophile membranes of these filters only by diffusion.

Then, the air pressure in line 508 increases, which is registered by a manometer 504. Pump 502 is driven until a positive air pressure of typically 1 bar (1000 hPa) has been built up. Then, the pump is stopped and the pressure relaxation curve is followed at the manometer 504. At intact sterile filter membranes, the pressure decreases slowly. If there is a leakage, the pressure decreases faster. The rate of decrease of pressure at which a membrane can be considered tight is dependent on the membrane and is predefined in a control and monitoring unit (not shown).

It is also possible to test the integrity of the dialyser membranes at the same time, if the dialyser lines 308 and 144 are connected to the dialyser 200 instead of the short-circuit portion 150 as shown in figure 3. The testing of the dialyser is however also possible in a device corresponding to figure 2. For testing the sterile filters in a device according to figure 1 or 3, the rinse valve 320 is opened and the second dialyser valve 125 is closed. Valves 122 and 124 can be positioned in an arbitrary position. Pump 502 is started and the testing process takes place as described above.

The dialyser valve 125 can be left out for the testing process if the throttle device has

the possibility to be completely closed. In this case, the throttle device is closed for the testing process. The simultaneous testing of the dialyser is not possible any longer. In this case, it is possible to arrange the bypass connector 314 in the area of the short circuit portion 150.

The device can be further modified. What is essential is that the area between the two filters during the test process is connected to the drain only through the membranes of the two filters. Also the pump 502 and the manometer 504 are not completely necessary. The test process can also takes place with an negative pressure at the dialysate side. Then, only the hydrophobe sterile filter 506 is necessary, which is open to the atmosphere. For testing, the valves are operated as described and by means of pump 120 or pump 130 plus an opened bleeding valve 132, a negative pressure is generated. Then, the fluid is pumped out of the area between the two sterile filters while at the same time air enters through the hydrophobe filter 506. When all fluid has left the area between the two sterile filters, the pressure in the area of the dialysate line 144 decreases, which can be sensed by the dialysate pressure sensor 126. When reaching a predetermined negative pressure, the pump 120 is stopped and the valve 132 is closed and the pressure increase can be determined in a known way for detecting leakages.

By means of the test process described, both sterile filters and possibly also the dialyser are tested for leakages. With the device according to figure 2, also a separate test of the two filters can be performed. The first sterile filter 302 is tested if valve 124 is closed and valve 122 is opened. The second sterile filter is separately tested if valve 122 is closed and valve 124 is opened. Then it is presumed that the balancing unit 100 does not permit any return flow.

The hydrophobe filter 506 is preferably adapted close to the connection 304 for making line 508 as short as possible. It is preferable if line 508 is removed and filter 506 is passed through tangentially. In each case, it is preferable that the test is performed before and after the disinfection operation. Then, the disinfection agent can reach the line 508 and then be removed again.

The sterile filters are disinfected together with the rest of the dialysis machine. Then, it has to be observed that disinfection agents and temperatures are used, which are compatible with the filter material. Thus, filters with membranes of polysulphone and polyvinylpyrolidone cannot be used together with an disinfection agent comprising sodium hypochlorite. For disinfection, the terminal of the substitution fluid line 332 including the anticontamination portion 334 is connected to the bypass connector 314. During disinfection, a positive pressure is maintained in the area of the sterile filters by the throttle device 310, whereby a portion of

the disinfection agent circulating in the fluid circuit passes through the filters.

Before start of the next treatment, the disinfection agent is rinsed off as usual. The substitution fluid line is disconnected from bypass connector 314 and connected to a new sterile intermediate portion 334 and connected to the venous drip chamber 244. The old intermediate portion 334 is discarded. The anticontamination intermediate portion 334 has the object to obviate a cross contamination at contact with the patient blood. Usually, the connection portion during the disinfection process is only sterilised at the inner surfaces. A contamination can, however, also take place via the outer surfaces, at the generally used Luer connectors. As intermediate portion is preferably used a non-return valve which is cheaply available from i.a. the infusion technique. This non-return valve can be provided with one or two additional tube portions. Also, the complete tube portion 330 can be made as a disposable article and the separate intermediate portion 334 is then unnecessary. This is specially advantageous if the second sterile filter 306 has only one connector at the filter side.

Several embodiments of the invention has been described above with reference to the drawings. The different features can be combined in further alternatives, and such combinations are intended to be within the scope of the invention. The invention is only limited by the appended patent claims.

PATENT CLAIMS:

1. Device for obtaining sterile infusion or substitution solution at hemodialysis, hemofiltration or hemodiafiltration with a device for balancing fresh and spent dialysis fluid and a throttle device, dividing the area of the fresh dialysis fluid in a positive pressure portion and a negative pressure portion and at least one sterile filter, **characterised** in that said sterile filter is adapted in the positive pressure area of the dialysis circuit.

2. Device according to claim 1, **characterised** in that the inlet area of the sterile filter is passed through by the dialysate.

3. Device according to claim 1 or 2, **characterised** in that another sterile filter is adapted in the inlet area and which is connected to the outlet via a throttle device and which filters essentially the entire dialysis fluid flow.

4. Device according to any one of claims 1 to 3, **characterised** in that the throttle device dividing the area of the fresh dialysis fluid in a positive pressure portion and a negative pressure portion is a constant pressure valve.

5. Device according to any one of claims 1 to 3, **characterised** in that the throttle device dividing the area of the fresh dialysis fluid in a positive pressure portion and a negative pressure portion is a constant flow valve.

6. Device according to any one of claims 1 to 3, **characterised** in that the throttle device dividing the area of the fresh dialysis fluid in a positive pressure portion and a negative pressure portion is an adjustable throttle device.

7. Device according to any one of claims 1-4, **characterised** in that a flow meter (312) is arranged in the dialysis fluid circuit between the sterile filter and the dialyser.

8. Device according to claim 7, **characterised** in that the flow meter is connected to a control device which can control the throttle device (310) so that a predetermined substitution flow is adjusted.

9. Device according to any one of the preceding claims, **characterised** in that there is arranged a device for testing the integrity of the sterile filters.

10. Device according to claim 9, **characterised** in that the device for testing comprises an air pump which can provide the area between the two sterile filters with air, and that there is arranged a stop valve downstream of the second filter as seen in the dialysis fluid circuit

flow.

11. Device according to claim 10, **characterized** in that the line from the air pump (502) to the dialysis fluid circuit between the sterile filters (304) comprises a hydrophobe sterile filter (506).

12. Device according to any one of claims 10-11, **characterised** in that the stop valve adapted downstream of the second filter is arranged downstream of the dialyser but upstream of the connector (314).

13. Device according to claim 5 and any one of claims 10-12, **characterised** in that the stop valve arranged downstream of the second sterile filter is the adjustable throttle device 310.

14. Device according to claim 9, **characterised** in that the device for testing the integrity of the sterile filters comprises a bleeding device by which the area between the sterile filters can be provided with air.

15. Method for testing sterile filters in a device according to claims 2 and 14, **characterised** in that a negative pressure is obtained with the ultrafiltration pump (120) or the dialysate circulation pump (130) and the pump is stopped when a predetermined pressure has been obtained and that the pressure curve is measured with the dialysate pressure sensor (126) and by means thereof the state of the sterile filters are obtained.

16. Device according to claim 1 for obtaining sterile substitution solution for treatment of a renal decease patient by hemodialysis, hemofiltration or hemodiafiltration, comprising:

a source for hemodialysis fluid;

a first pumping device for pumping said hemdialysis fluid via a first line to a dialysing device, such as a dialyser, a hemofilter or a hemodiafilter;

a throttling device positioned in said first line between the pumping device and the dialysing device;

a branch line comprising a sterile filter and being connected to the first line between said pumping device and said throttling device and terminating in an extracoporeal circuit comprising blood from the patient to be treated;

characterised by control means for controlling the throttle device for maintaining a predetermined substitution fluid flow rate through said branch line.

17. Device according to claim 16, **characterized** in that said throttle device is an adjustable throttle valve or an adjustable three-way valve.

18. Device according to claim 17, **characterized** in that said control means comprises a flow meter positioned in said first line between the connection of the branch line and the dialyser for measuring the dialysis fluid flow to the dialyser, said control means controlling said adjustable valve for obtaining said predetermined substitution fluid flow through said branch line as the difference between the dialysis fluid flow obtained by the first pumping device and said flow meter measurement.

19. Device according to claim 16, **characterized** in that said first pumping device is an adjustable constant flow pump, passing a predetermined dialysis fluid flow rate, and that said throttle device is an adjustable constant flow pump, passing a predetermined amount of fluid which is the difference between the dialysis fluid flow rate and the predetermined substitution fluid flow rate.

20. Method for obtaining a sterile substitution solution for treatment of a renal decease patient by hemodialysis, hemofiltration or hemodiafiltration, comprising:

providing a hemodialysis fluid;

pumping said hemdialysis fluid via a first line to a dialysing device, such as a dialyser, a hemofilter or a hemodiafilter by a first pumping device;

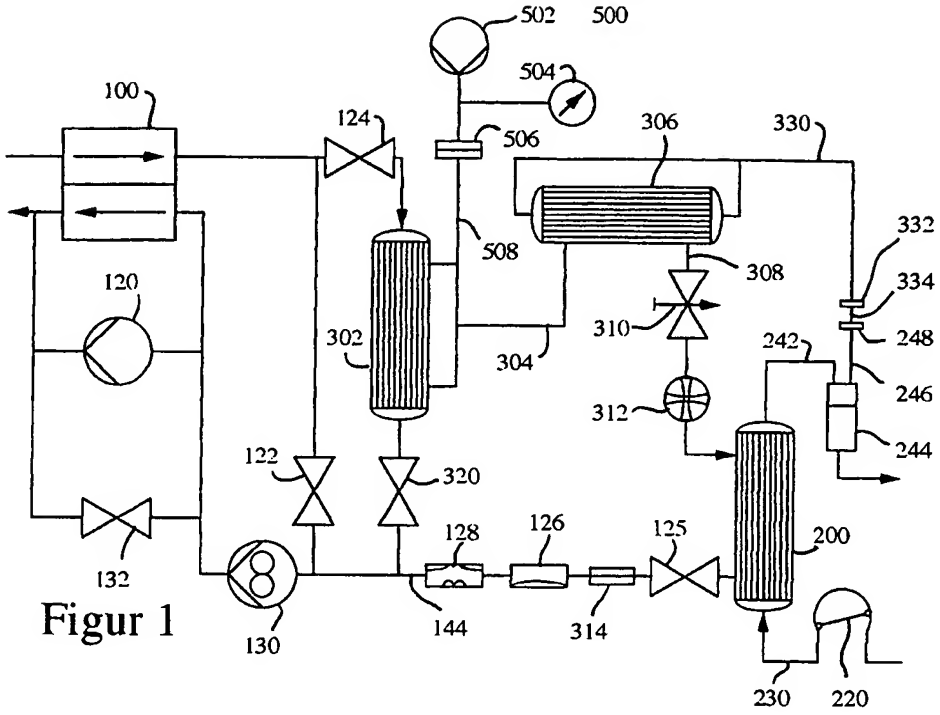
providing a throttling device in said first line between the pumping device and the dialysing device for providing an increased pressure;

obtaining a substitution solution in a branch line comprising a sterile filter and being connected to the first line between said pumping device and said throttling device;

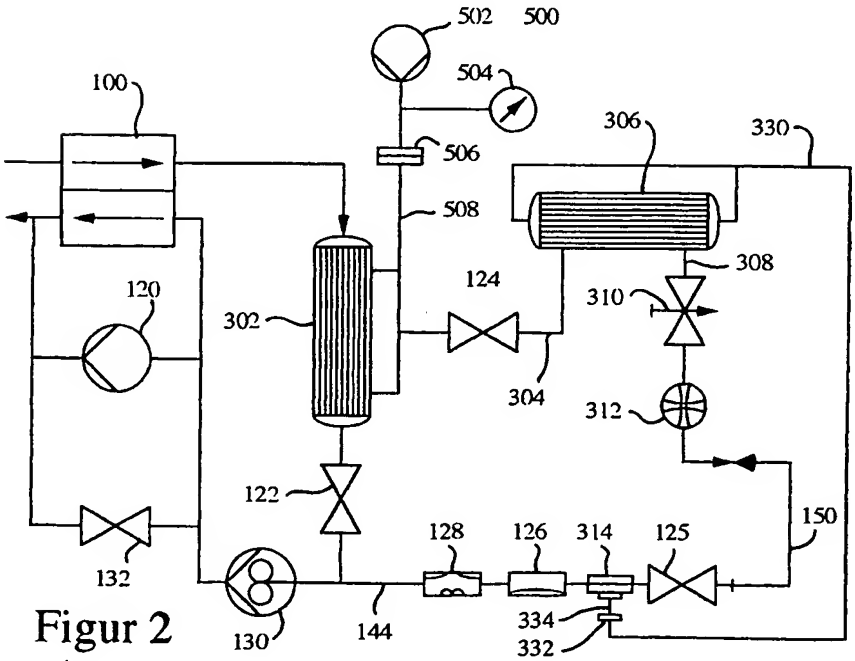
passing said substitution fluid to an extracoporeal circuit comprising blood from the patient to be treated;

characterised by controlling the throttle device for maintaining a predetermined substitution fluid flow rate through said branch line.

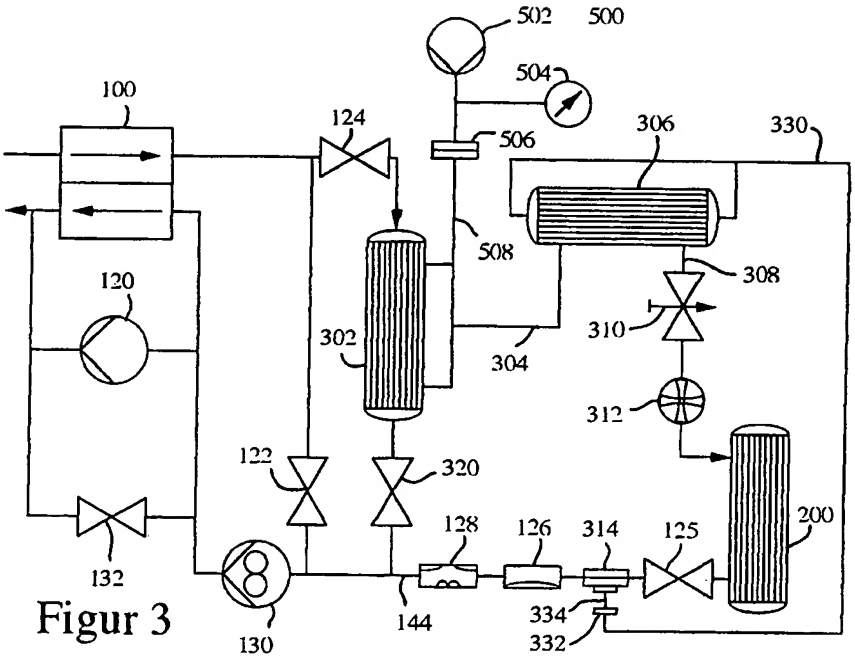
21. Device according to claim 20, **characterized** by measuring the dialysis fluid flow to the dialyser by a flow meter positioned in said first line between the connection of the branch line and the dialyser, and adjusting said throttle device for obtaining said predetermined substitution fluid flow through said branch line as the difference between the dialysis fluid flow obtained by the first pumping device and said flow meter measurement.



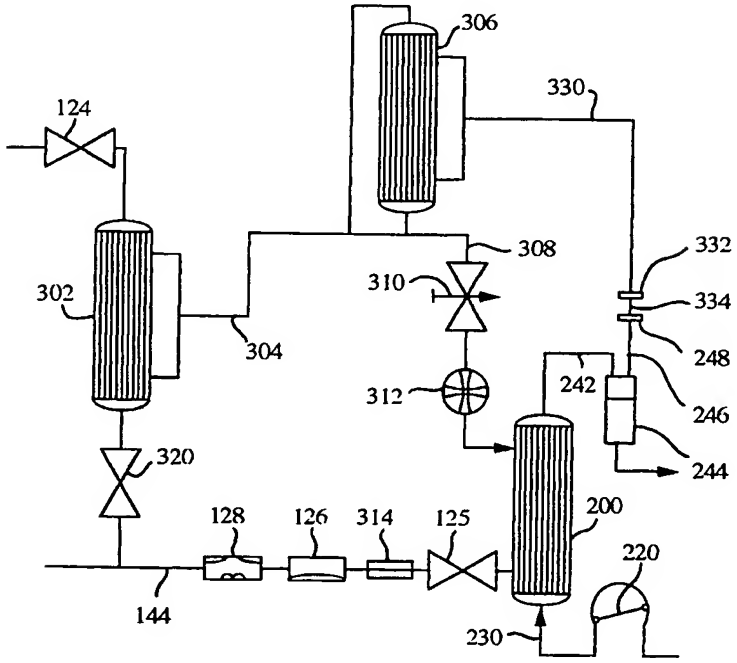
Figur 1



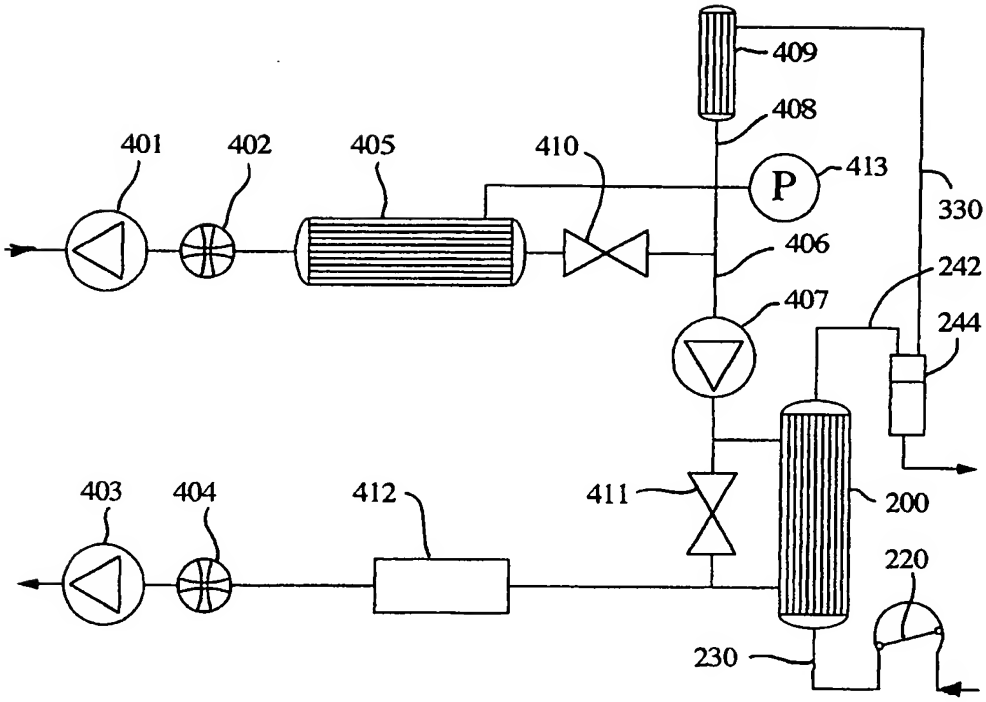
Figur 2



Figur 3



Figur 4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Figur 5

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 98/00005

A. CLASSIFICATION OF SUBJECT MATTER

IPC6: A61M 1/34, A61M 1/16
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC6: A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPI

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0694312 A2 (HOSPAL INDUSTRIE), 31 January 1996 (31.01.96), column 9, line 36 - column 10, line 37, figure 2	1-21
A	EP 0692269 A2 (FRESENIUS AG), 17 January 1996 (17.01.96), column 4, line 49 - column 5, line 57	1-21
A	US 5476592 A (L. SIMARD), 19 December 1995 (19.12.95), column 1, line 55 - column 2, line 37	1-21
A	US 4708802 A (D. RATH ET AL.), 24 November 1987 (24.11.87), column 3, line 29 - line 68	1-21

[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" erlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 May 1998	15 -05- 1998
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Eva Selin Telephone No. +46 8 782 25 00

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE.98/00005

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4209391 A (B.J. LIPPS ET AL.), 24 June 1980 (24.06.80), column 9, line 4 - line 26 -- ---------	1-21

INTERNATIONAL SEARCH REPORT

Information on patent family members

29/04/98

International application No.
PCT/SE 98/00005

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